

CLAIMS:

1. A GLP-1 peptide comprising the following formula, or a pharmaceutically acceptable salt thereof:

X-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-val-Lys-Gly-Arg-Y (SEQ ID NO.1)

wherein:

X is a rigidifying hydrophobic moiety selected from the group consisting of:

- i. C₁-C₁₀ alkenoic acid, wherein said alkenoic acid is not *trans*-3-hexenoic acid and wherein said alkenoic acid is substituted by at least one substituent selected from the group consisting of straight or branched C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl and substituted aryl;
- ii. C₁-C₁₀ alkynoic acid;
- iii. C₃-C₁₀ cycloalkanoic acid or heterocycloalkanoic acid, wherein the heterocycloalkanoic acid comprises an heteroatom selected from the group consisting of O, S and N;
- iv. C₅-C₁₄ arylcarboxylic or arylalkanoic acid, wherein the arylcarboxylic or arylalkanoic acid is substituted by at least one substituent selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halo, hydroxy, trifluoromethyl, amino, -NH(lower alkyl), -N(lower alkyl)₂, di- and tri-substituted phenyl, 1-naphthyl, and 2-naphthyl wherein said di- and tri-substituted phenyl, 1-naphthyl, and 2-naphthyl are substituted with a substituent selected from the group consisting of methyl,

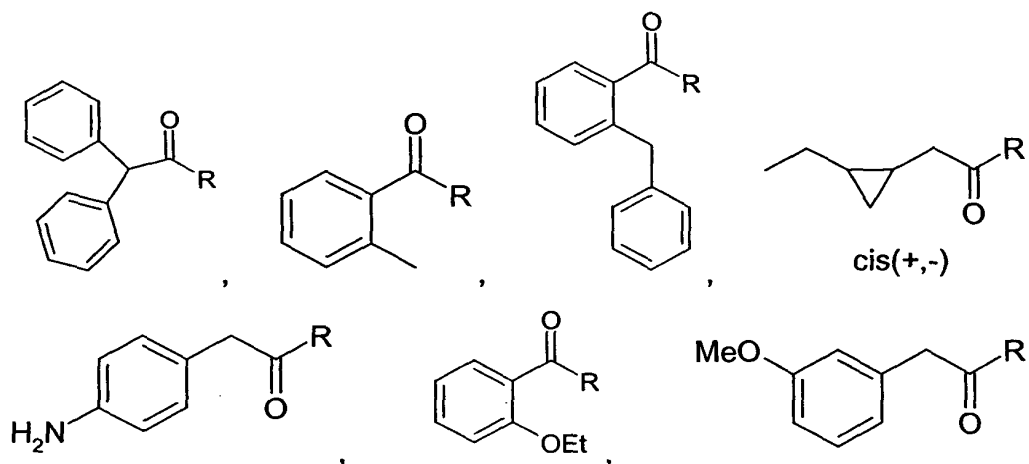
methoxy, methylthio, halo, hydroxy, and amino;

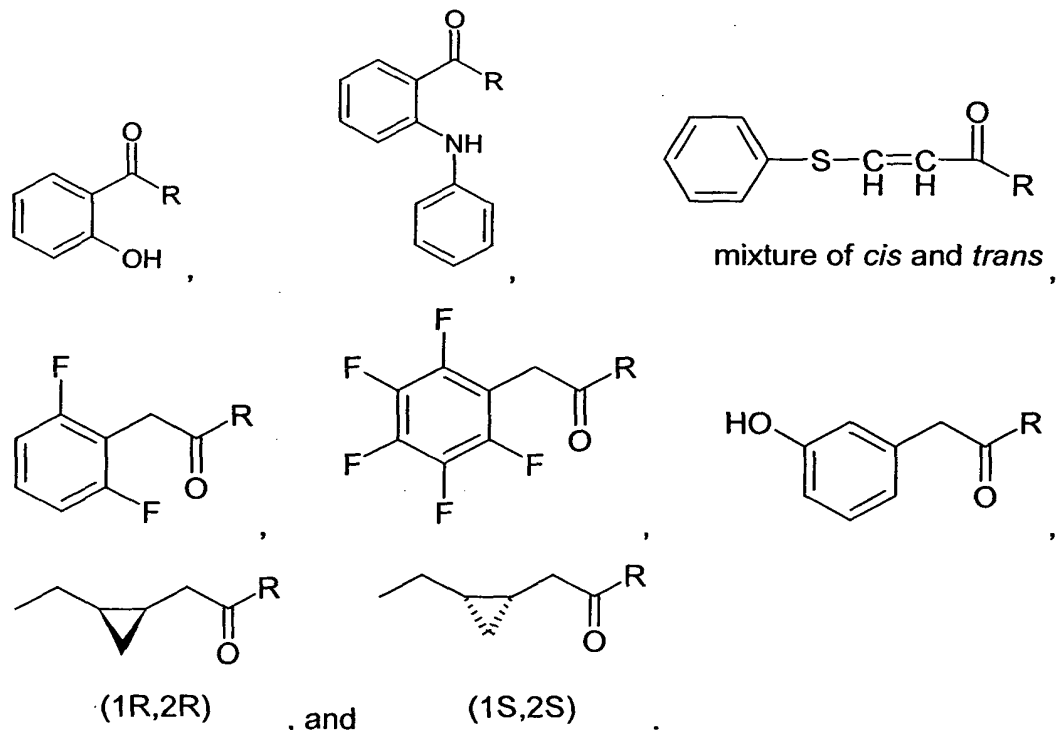
v. C_5 - C_{14} heteroarylcarboxylic or heteroarylalkanoic acid wherein the heteroarylcarboxylic or heteroarylalkanoic acid comprises a heteroatom selected from the group consisting of O, S and N, and wherein the heteroarylcarboxylic or heteroarylalkanoic acid is substituted by at least one substituent from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halo, hydroxy, trifluoromethyl, amino, -NH(lower alkyl), -N(lower alkyl)₂, di- and tri-substituted phenyl, 1-naphthyl, and 2-naphthyl, wherein said di- and tri-substituted phenyl, 1-naphthyl, or 2-naphthyl are substituted with a substituent selected from the group consisting of methyl, methoxy, methylthio, halo, hydroxy, and amino;

and

Y is selected from the group consisting of OH, NH₂ and Gly-OH.

2. The peptide of claim 1, wherein X is selected from the group consisting of:





3. The peptide of claim 1, wherein X is selected from the group consisting of 3-aminophenyl acetyl, 3-methoxyphenyl acetyl, salicyl, (1R, 2R) 2-ethylcyclopropyl acetyl, and (1S, 2S) 2-ethylcyclopropyl acetyl.

4. A composition comprising a therapeutically effective amount of a peptide of claim 1, or a pharmaceutically acceptable salt thereof, in association with at least one constituent selected from the group consisting of pharmaceutically acceptable carrier, diluent, and excipient.

5. The composition of claim 4, wherein said therapeutically effective amount is comprised between about 1 mcg and about 10 mg.

6. A method for treating or preventing a disease or condition associated with a disorder of glucose metabolism comprising administering to a subject in need thereof a therapeutically effective

amount of the peptide of claim 1.

7. The method of claim 6, wherein said disease or condition associated with a disorder of glucose metabolism is selected from diabetes mellitus of Type I or Type II and insulin resistance.

8. The method of claim 7, wherein said condition is diabetes mellitus of Type I or Type II.

9. The method of claim 7, wherein said condition is insulin resistance.

10. The method of claim 6, wherein said disease or condition is a weight disorder or associated condition.

11. The method of claim 10, wherein said weight disorder or associated condition is selected from at least one of lowering weight, increasing satiety, post-prandially increasing plasma insulin levels, reducing blood glucose levels, and increasing pancreatic beta cell mass in said subject.

12. The method of claim 11, wherein said lowering weight is from about 1 to about 10 kg.

13. The method of claim 11, wherein said increasing satiety is of the order of about 10%.

14. The method of claim 11, wherein said post-prandially increasing plasma insulin levels is of the order of about 10%.

15. The method of claim 11, wherein said reducing blood glucose levels is of the order of about 10%.

16. The method of claim 11, wherein said increasing pancreatic beta cell mass is of at least about 10%.

17. The method of claim 6, wherein said peptide, or pharmaceutically acceptable salt thereof, is administered to said subject through an administration route selected from the group consisting of subcutaneous, intravenous, transdermal, oral, buccal and intranasal.

18. The method of claim 6, wherein said subject is a human.

19. A composition comprising a prophylactically effective amount of a peptide of claim 1, or a pharmaceutically acceptable salt thereof, in association with at least one constituent selected from the group consisting of pharmaceutically acceptable carrier, diluent and excipient.